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09/493,022	01/27/2000	Jeffrey Skolnick	10886-045001	1668

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EXAMINER

CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 10/20/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/493,022

Applicant(s)

SKOLNICK ET AL.

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 9-25 is/are pending in the application.
- 4a) Of the above claim(s) 9-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Applicant's arguments filed 7 July 2003 have been fully considered but they are not persuasive, for reasons set forth below. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 9-25 are currently pending.

This application contains claims 9-13 drawn to an invention nonelected without traverse in Paper No. 8. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 14-25 are rejected under 35 U.S.C. 102(a) as being anticipated by Kolinski et al. (Proceedings of HRCL Workshop on Monte Carlo Approach to Biopolymers and Protein Folding. P. Grassberger et al., Eds., World Scientific, Singapore/London, pages 100-130).

Applicant argues that claims 14-25 are not described in Kolinski (HRCL Workshop). In particular, Applicant avers that Kolinski does not teach the computer-assisted method for determining a three-dimensional structure of a target amino acid sequence by aligning a target amino-acid sequence with a template amino acid sequence and producing from the alignment a

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three-dimensional reduced protein model comprising representations of side chains of amino acid residues comprising a target protein, wherein said representations of side chains of amino acid residues are converted to interaction centers and each interaction center comprises a pseudoatom representing a center of mass of the side chain of the represented amino acid to which the interaction center corresponds, and each interaction center is connected to an immediately proximal interaction center and an immediately distal interaction center via a virtual covalent bond to produce an interaction center chain, which is projected onto an underlying cubic lattice to produce a projected chain of interaction centers, and the secondary constraints and/or tertiary constraints are applied to a subset of, or all of, the interaction centers of the interaction center chain to generate a force field comprising short-range interactions, thereby producing a data set representing a three-dimensional model structure of the target protein (page 9, 3<sup>rd</sup> paragraph of response).

Applicant further states that Kolinski does not produce an interaction center chain and project the interaction center chain onto an underlying cubic lattice to produce a projected chain of interaction centers by using a calculated force field comprising short-range interactions as set forth in the specification.

However, these arguments are not persuasive, as Kolinski clearly teaches all of the embodiments of the instant invention, as stated in the previous Office Action. Kolinski clearly sets forth a system for reduced models of proteins based upon a lattice model of protein structure prediction. Kolinski outlines the basic premise of the design and elaborates on several modifications that can be made to implement protein structure prediction utilizing a computer. In particular, he describes the lattice model approach as having several advantages, such as

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enabling more efficient computations due to smaller number of conformations being considered (page 110, 3<sup>rd</sup> paragraph). He describes both long and short-range interaction models (page 111 and page 119, respectively). He describes in great detail the use of the interaction center which represents a center of mass of the side chain of amino acids (page 114-116). He goes on to describe the restraints which are superimposed on the top of a more general force field model which consists of short-range interactions and long-range interactions (page 120) generated from model proteins for the identification of a target (p. 121). The data sets utilized produced a three-dimensional model of a target protein, as illustrated in Figures 7-10.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "knowledge based origin" of a force field) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

It is also noted that Figure 3 in Kolinski et al. is identical to instant Figure 3, showing the method of projection onto a cubic lattice.

The rejection of claims 14-23 is maintained. Claims 24 and 25 are newly rejected.

Claims 14-25 are rejected under 35 U.S.C. 102(a) as being anticipated by Kolinski et al. (J. Phys. Chem. (1998) Vol. 102, pages 4628-4637).

Applicant argues that claims 14-25 are not described in Kolinski (J. Phys. Chem). In particular, Applicant avers that Kolinski does not teach the computer-assisted method for determining a three-dimensional structure of a target amino acid sequence by aligning a target

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amino-acid sequence with a template amino acid sequence and producing from the alignment a three-dimensional reduced protein model comprising representations of side chains of amino acid residues comprising a target protein, wherein said representations of side chains of amino acid residues are converted to interaction centers and each interaction center comprises a pseudoatom representing a center of mass of the side chain of the represented amino acid to which the interaction center corresponds, and each interaction center is connected to an immediately proximal interaction center and an immediately distal interaction center via a virtual covalent bond to produce an interaction center chain, which is projected onto an underlying cubic lattice to produce a projected chain of interaction centers, and the secondary constraints and/or tertiary constraints are applied to a subset of, or all of, the interaction centers of the interaction center chain to generate a force field comprising short-range interactions, thereby producing a data set representing a three-dimensional model structure of the target protein (page 11, 2<sup>nd</sup> paragraph of response).

Applicant further states that Kolinski does not produce an interaction center chain and project the interaction center chain onto an underlying cubic lattice to produce a projected chain of interaction centers by using a calculated force field comprising short-range interactions as set forth in the specification.

However, these arguments are not persuasive, and even confusing, in that Applicant points out clearly the teachings of Kolinski that exemplify the claims in the instant application. Kolinski states, "The purpose of this work is to analyze the role of the generic protein-like regularities seen on protein chains, the role of sequence-specific short-range correlations of the side-chain positions and this interplay". Applicant is only arguing that Kolinski does not

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produce an interaction center chain etc. (as stated above). However, it is clear that Kolinski does teach the production of an interaction center based upon the centers of mass of side chains. He states, "it is easy to define a center of mass for a given rotational isomeric side chain" and goes on to explain the method in detail (see page 4629, beginning column 1). "The chains consist of united atoms restricted to an underlying simple cubic lattice. The distance between the two successive units of such a chain depends on the identity of the corresponding residues and the actual rotameric state of their side chains...If each pair of two clusters is not allowed to overlap, the resulting hard core is characterized by a distance of closet approach equal to 3 lattice units...The lattice representation provides a very convenient way for modeling excluded volume and detecting nearest neighbors and the stochastic simulation of the chain dynamics..." It is clear that Kolinski teaches the embodiments of the claimed instant invention of lattice representation of polypeptide chains.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "knowledge based origin" of a force field) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The rejection of claims 14-23 is maintained. Claims 24 and 25 are newly rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

### *Inquiries*

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

*Lori A. Clow*  
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MARJORIE MORAN  
PATENT EXAMINER

*Marjorie A. Moran*